



PATENT  
ATTORNEY DOCKET NO. STEM1110-5

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Twardzik et al.  
Serial No.: 10/050,190  
Filed: January 15, 2002  
Title: TGF- $\alpha$  POLYPEPTIDES, FUNCTIONAL FRAGMENTS AND METHODS OF  
USE THEREFOR

Art Unit: 1647  
Examiner To be assigned

#5  
1647  
12/5/02

Commissioner for Patents  
Washington, D.C. 20231

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INFORMATION DISCLOSURE STATEMENT

Sir:

In accordance with 37 CFR 1.97, enclosed is a list of references relating to the above-identified application. For the convenience of the Examiner, these references are listed on the attached Form PTO-1449.

In accordance with 37 C.F.R. 1.97, Applicant brings to the Examiner's attention the related parent patent application, U.S. Serial No. 09/641,587 filed August 17, 2000, which is relied upon for an earlier filing date under 35 U.S.C. § 120. As the references on the enclosed Form PTO-1449 were submitted in an application relied upon for an earlier filing date, copies of the cited references are not enclosed, pursuant to 37 CFR 1.98(d). Copies of the documents will be found in the above-referenced parent application.

**CERTIFICATION UNDER 37 CFR §1.8**

I hereby certify that the documents referred to as enclosed herein are being deposited with the United States Postal Service as first class mail on this date, November 21, 2002 in an envelope addressed to:  
Commissioner for Patents, Washington, D.C. 20231.

Jason Berry

Name of Person Mailing Paper

Signature

In the Application of  
Twardzik et al.  
Application Serial No.: 10/050,190  
Filed: January 15, 2002

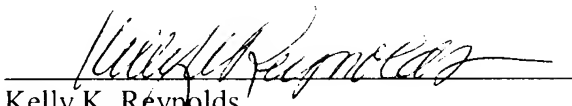
PATENT  
Attorney Docket No.: STEM1110-5

It is respectfully requested that these references be considered in the examination of this application and their consideration be made of written record in the application file.

This Information Disclosure Statement is being filed prior to receipt of a First Office Action on the merits. Therefore, no fee is deemed necessary. However, the Commissioner is hereby authorized to charge any amounts required by this filing, or credit any overpayment, to Deposit Account No. 50-1355.

Respectfully submitted,

Date: 11/21/02

  
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**United States Patent & Trademark Customer No. 28213**



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TRANSMITTAL SHEET

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Sir:

Transmitted herewith for the above-identified application, please find:

- (1) An Information Disclosure Statement (2 pages);
- (2) A Form PTO-1449 (9 pages); and
- (3) Return postcard;

**CERTIFICATION UNDER 37 CFR §1.8**

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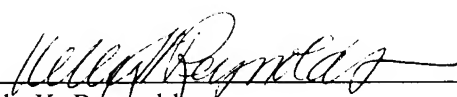
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**U.S. PATENT DOCUMENTS**

EXAM. INITIALS		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB- CLASS	FILING DATE
	AA	4,742,003	05/03/1988	Derynck and Goeddel			
	AB	4,749,683	06/07/1988	Murphy and Rhodes			
	AC	4,863,899	09/05/1989	George J. Todaro			
	AD	4,863,902	09/05/1989	Amagase et al			
	AE	4,874,746	10/17/1989	Antoniades and Lynch			
	AF	5,102,870	04/7/1992	Florine and Smith			
	AG	5,229,493	07/20/1993	Folkman et al.			
	AH	5,328,986	07/12/1994	Folkman and Shing			
	AI	5,750,376	05/12/1998	Weiss et al.			
	AJ	5,814,308	09/29/1998	Ke Zhang			
	AK	5,851,832	12/22/1998	Weiss et al.			
	AL	5,885,956	03/23/1999	Nardi and Brand			
	AM	5,886,141	03/23/1999	Folkman et al.			
	AN	5,902,799	05/11/1999	Herrmann et al.			
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	AP	5,981,165	11/09/1999	Weiss and Reynolds			

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EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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	AQ	6,011,004	01/04/2000	Kessler and Apfel			
	AR	6,013,762	01/11/2000	Folkman et al.			
	AS	6,071,889	06/06/2000	Weiss et al.			
	AT	6,114,307	09/05/2000	Jaspers et al.			
	AU	6,232,288 B1	05/15/2001	Itaru Kojima			
	AV	6,288,301 B1	09/11/2001	Nardi and Brand			
	AW	6,326,201 B1	12/04/2001	Fung et al.			

### FOREIGN PATENT DOCUMENTS

EXAM. INITIALS		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB- CLASS	TRANSLATION (YES/NO)
	AX	WO 84/01106	03/29/1984	PCT			
	AY	0 154 434 A1	09/11/1985	EP			
	AZ	WO 94/16718	08/04/1994	PCT			
	BA	WO 98/22127	05/28/1998	PCT			
	BB	WO 99/06060	02/11/1999	PCT			
	BC	WO 00/44400	08/03/2000	PCT			

### OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages)

	BD	Blikslager, Anthony T. et al., "Glutamine and Transforming Growth Factor- $\alpha$ Stimulate Extracellular Regulated Kinases and Enhance Recovery of Villous Surface Area In Porcine Ischemic-Injured Intestine," <i>Surgery</i> , Vol. 125, No. 2, February 1999, pgs. 186-194.
	BE	Blikslager, A.T. et al., "Glutamine and Transforming Growth Factor Alpha Enhance Repair of Intestinal Ischemia/Reperfusion Injury," <i>Supplement to Gastroenterology</i> , Vol. 110, No. 4, April 1996, Abstract pg. A313.
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BG	Burgel, Pierre-Regis et al., "Human Eosinophils Induce Mucin Production In Airway Epithelial Cells Via Epidermal Growth Factor Receptor Activation," <i>The Journal of Immunology</i> , 2001, pgs. 5948-5954.
BH	Carpenter, Graham et al., "Antibodies to the Epidermal Growth Factor Recptor Block the Biological Activities of Sarcoma Growth Factor," <i>Proc. Natl. Acad. Sci. USA</i> , Vol. 80, September 1983, pgs. 5627-
BI	Chamberlin, Stephen G. et al., "Constrained Peptide Analogues of Transforming Growth Factor- $\alpha$ Residues Cysteine 21-32 Are Mitogenically Active," <i>The Journal of Biological Chemistry</i> , Vol. 270, No. 36, September 8, 1995, pgs. 21062-21067.
BJ	Chosidow, O. et al., "Tripe Palms Associated With Systemic Mastocytosis: The Role of Transforming Growth Factor- $\alpha$ and Efficacy of Interferon-Alfa," <i>British Journal of Dermatology</i> , Vol. 138, 1998, pgs. 698-703.
BK	Chou and Fasman, "Prediction of Protein Conformation," <i>Biochemistry</i> , Vol. 13, No. 2, 1974, pgs. 222-245.
BL	Coffey, Robert J. et al., "Transforming Growth Factors and Related Peptides in Gastrointestinal Neoplasia," <i>Journal of Cellular Biochemistry</i> , Supplement 16G, 1992, pgs. 111-118.
BM	Dayhoff, M.O. et al., "A Model of Evolutionary Change in Proteins," <i>Atlas of Protein Sequence and Structure</i> , 1972, pgs. 89-99.
BN	De Larco, Joseph E. et al., "Sarcoma Growth Factor from Mouse Sarcoma Virus-Transformed Cells," <i>The Journal of Biological Chemistry</i> , Vol. 255, No. 8, April 25, 1980, pgs. 3685-3690.
BO	Draoui, Muriel et al., "TGF $\alpha$ -PE40 Inhibits Non-Small Cell Lung Cancer Growth," <i>Life Sciences</i> , Vol. 54, No. 7, 1994, pgs. 445-453.
BP	Dunbar and Goddard, "Structure-function and Biological Role of Betacellulin," <i>The International Journal of Biochemistry &amp; Cell Biology</i> , Vol. 32, 2000, pgs. 805-815.

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BQ	Ebadi, M. et al., "Neurotrophins and Their Receptors In Nerve Injury and Repair," <i>Neurochem. Int.</i> , Vol. 30, Nos. 4/5, 1997, pgs. 347-374.
BR	Egger, B. "Reduced Susceptibility of Mice Overexpressing Transforming Growth Factor $\alpha$ To Dextran Sodium Sulphate Induced Colitis," <i>Gut</i> , Vol. 43, 1998, pgs. 64-70.
BS	Faber-Elman, A. et al., "Involvement of Wound-Associated Factors In Rat Brain Astrocyte Migratory Response to Axonal Injury In Vitro Simulation," <i>J. Clin. Invest.</i> , Vol. 97, No. 1, January 1996, pgs. 162-171.
BT	Ferrar, Isidre et al., "Transforming Growth Factor- $\alpha$ (TGF- $\alpha$ ) and Epidermal Growth Factor-Receptor (EGF-R) Immunoreactivity In Normal and Pathologic Brain," <i>Progress In Neurobiology</i> , Vol. 49, 1996, pgs. 99-123.
BU	Ghielli, Manuela et al., "Regeneration Processes In the Kidney After Acute Injury: Role of Infiltrating Cells," <i>Exp. Nephrol.</i> , Vol. 6, 1998, pgs. 502-507.
BV	Hardie, William D. et al., "Dose-Dependent Lung Remodeling In Transgenic Mice Expressing Transforming Growth factor- $\alpha$ ," <i>Am. J. Physiol. Lung Cell. Mol. Physiol.</i> , Vol. 281, 2001, pgs. L1088-L1094.
BW	Hardie, William D. et al., "Attenuation of Acute Lung Injury In Transgenic Mice Expressing Human Transforming Growth factor- $\alpha$ ," <i>Am. J. Physiol.</i> , Vol. 277, 1999, pgs. L1045-L1050.
BX	Heidenkummer and Kampik, "Immunohistochemical Localization of Epidermal Growth Factor Receptor In A Human Epiretinal Membrane," <i>Graefe's Arch. Clin. Exp. Ophthalmol.</i> , Vol. 229, 1991, pgs. 492-496.
BY	Ibbotson, K.J. et al., "Tumor-Derived Growth Factor Increases Bone Resorption in A Tumor Associated with Humoral Hypercalcemia of Malignancy," <i>Science</i> , Vol. 221, pgs. 1292-1294.
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CA	Jackson, Bruce A. et al., "Effects of transforming Growth Factor $\beta$ and Interleukin-1 $\beta$ on Expression of Cyclooxygenase 1 and 2 and Phospholipase A <sub>2</sub> mRNA In Lung Fibroblasts and Endothelial Cells in Culture," <i>Biochemical and Biophysical Research Communications</i> , Vol. 197, No. 3, December 30, 1993, pgs. 1465-1474.
CB	Jayaraman, Gurunathan et al., "Conformational Studies of a Synthetic Cyclic Decapeptide Fragment of Rat Transforming Growth Factor- $\alpha$ ," <i>Int. J. Peptide Protein Res.</i> , Vol. 46, 1995, pgs. 88-96.
CC	Jones, M.K. et al., "Gastrointestinal Mucosal Regeneration: Role of Growth Factors," <i>Frontiers in Bioscience</i> , Vol. 4, March 15, 1999, pgs. d303-309.
CD	Kheradmand, Farrah et al., "Transforming Growth Factor- $\alpha$ Enhances Alveolar Epithelial cell Repair In a New In Vitro Model," <i>Am. J. Physiol.</i> , Vol. 267, 1994, pgs. L728-L738.
CE	Kobayashi, Kenzo et al., "The Mechanisms of Gastrointestinal Mucosal Injury and Repair," <i>Japanese Journal of Clinica</i> , Vol. 56, No. 9, September 15, 1998, pgs. 7 (2215)-14 (2222) (English abstract).
CF	Konturek, Peter Ch. Et al., "Epidermal Growth Factor and Transforming Growth Factor- $\alpha$ : Role In Protection and Healing of Gastric Mucosal Lesions," <i>European Journal of Gastroenterology &amp; Hepatology</i> , Vol. 7, 1995, pgs. 933-938.
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CH	Kornblum, Harley I. et al., "Prenatal Ontogeny of the Epidermal Growth Factor Receptor and Its Ligand, Transforming Growth Factor Alpha, in the Rat Brain," <i>The Journal of Comparative Neurology</i> , Vol. 380, 1997, pgs. 243-261.
CI	Kudlow, Jeffrey E. et al., "Inability of Anti-Epidermal Growth Factor Receptor Monoclonal Antibody to Block "Autocrine" Growth Stimulation in Transforming Growth Factor-Secreting Melanoma Cells," <i>The Journal of Biological Chemistry</i> , Vol. 259, No. 19, October 10, 1984, pgs. 11895-11900.
CJ	Lefebvre, Ph. P. et al., "Regeneration of the Neurosensory Structures in the Mammalian Inner Ear," <i>Acta. Oto-rhino-laryngologica belg.</i> , Vol. 51, 1997, pgs. 1-10.

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CK	Leong, Hoyee et al., "Cytostatic Effects of 3,3'-Diindolylmethane In Human Endometrial Cancer Cells Result from an Estrogen Receptor-Mediated Increase in Transforming Growth Factor- $\alpha$ Expression," <i>Carcinogenesis</i> , Vol. 22, No. 11, 2001, pgs. 1809-1817.
CL	Liu, Dan et al., "TGF- $\alpha$ Can Act as Morphogen and/or Mitogen in a Colon-Cancer Cell Line," <i>Int. J. Cancer</i> , Vol. 56, 1994, pgs. 603-608.
CM	Liu, Mark C. et al., "Allergy, Rhinitis, other Respiratory Diseases: Effects of Prednisone On the Cellular Responses and Release of Cytokines and Mediators After Segmental Allergen Challenge of Asthmatic Subjects," <i>Journal of Allergy and Clinical Immunology</i> , Vol. 108, No. 1, July 2001, 16 pages.
CN	Liu, Ming et al., "Immunohistochemical Study of Transforming Growth Factor-Alpha in Human Lung Cancers," <i>Tumor Biol.</i> , Vol. 13, 1992, pgs. 294-298.
CO	Lord, Bl. Et al., "Kinetics of Neutrophil Production in Normal and Neutropenic Animals During the Response to Filgrastim (r-metHu G-CSF) Filgrastim SD/01 (PEG-r-metHu G-CSF)," <i>Clin. Cancer Res.</i> , Vol. 7 July 2001, pgs. 2085-2090.
CP	Marquardt and Todaro, "Purification and Primary Structure of a Polypeptide with Multiplication-Stimulating Activity from Rat Liver Cell Cultures," <i>The Journal of Biological Chemistry</i> , Vol. 256, No. 13, July 10, 1981, pgs. 6859-6865.
CQ	Marquardt, Hans et al., "Transforming Growth Factors Produced By Retrovirus-Transformed Rodent Fibroblasts and Human Melanoma Cells: Amino Acid Sequence Homology with Epidermal Growth Factor," <i>Proc. Natl. Acad. Sci. USA</i> , Vol. 80, August 1983, pgs. 4684-4688.
CR	Miettinen, Paivi J., "Transforming Growth Factor- $\alpha$ and Epidermal Growth Factor Expression in Human Fetal Gastrointestinal Tract," <i>Pediatric Research</i> , Vol. 33, No. 5, 1993, pgs. 481-486.
CS	Mogi, Makio et al., "Interleuken-1 $\beta$ , Interleukin-6, Epidermal Growth Factor and Transforming Growth Factor- $\alpha$ are Elevated in the Brain from Parkinsonian Patients," <i>Neuroscience Letters</i> , Vol. 180, 1994, pgs. 147-150.

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CT	Nestor, Jr., John J. et al., "A Synthetic Fragment of Rat Transforming Growth Factor $\alpha$ with receptor Binding and Antigenic Properties," <i>Biochemical and Biophysical Research Communications</i> , Vol. 129, No. 1, May 31, 1985, pgs. 226-232.
CU	Ozanne, Brad et al., "Kirsten Murine Sarcoma Virus transformed Cell Lines and a Spontaneously Transformed rat Cell-Line Produce Transforming Factors," <i>Journal of Cellular Physiology</i> , Vol. 105, 1980, pgs. 163-180.
CV	Reid, S. et al., "Radial Migration of Subependymal Cells in the Adult Rodent Forebrain," <i>Society for Neuroscience</i> , Vol. 22, 1996, pg. 1956 (Abstract).
CW	Rimaniol, Anne-Cecile et al., "Biphasic Transforming Growth Factor- $\beta$ Production Flanking the Pro-Inflammatory Cytokine Response in Cerebral Trauma," <i>NeuroReport</i> , Vol. 7, 1995, pgs. 133-136.
CX	Romano, Marco et al., "Transforming Growth Factor $\alpha$ Protection Against Drug-Induced Injury to the Rat Gastric Mucosa In Vivo," <i>J. Clin. Invest.</i> , Vol. 90, 1992, pgs. 2409-2421.
CY	Rudinger, J., "Characteristics of the Amino Acids as Componentes of a Peptide Hormone Sequence," <i>Biological Council: Peptide Hormones</i> , June 1976, pgs. 1-7.
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DB	Scheiman, James M. et al., "Transforming Growth Factor-Alpha (TGF- $\alpha$ ) Levels in Human Proximal Gastrointestinal Epithelium: Effects of Mucosal Injury and Acid Inhibition," <i>Digestive Diseases and Sciences</i> , Vol. 42, No. 2, February 1997, pgs. 333-341.
DC	Schultz and Twardzik, "Assessment of Biological Activity of Synthetic Fragments of transforming Growth Factor $\alpha$ ," <i>Methods In Enzymology</i> , Vol. 198, 1991, pgs. 200-213.
DD	Shing, Y. et al., "Betacellulin: A Mitogen from Pancreatic $\beta$ Cell Tumors," <i>Science</i> , Vol. 259, March 12, 1993, pgs. 1604-1607.

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DF	Song, Si young et al., "Expansion of Pdx1-Expressing Pancreatic Epithelium and Islet Neogenesis in Transgenic Mice Overexpressing Transforming Growth Factor $\alpha$ ," <i>Gastroenterology</i> , Vol. 117, 1999, pgs. 1416-1426.
DG	Sottili, Mauro et al., "Up-Regulation of Transforming Growth Factor $\alpha$ Binding Sites in Experimental Rabbit Colitis," <i>Gastroenterology</i> , Vol. 109, 1995, pgs. 24-31.
DH	Sporn and Todaro, "Autocrine Secretion and Malignant Transformation of Cells," <i>The New England Journal of Medicine</i> , Vol. 303, No. 15, October 9, 1980, pgs. 878-880.
DI	Subauste and Proud, "Effects of Tumor Necrosis Factor- $\alpha$ , Epidermal Growth Factor and Transforming Growth Factor- $\alpha$ on Interleukin-8 Production By, and Human Rhinovirus Replication in, Bronchial Epithelial Cells," <i>International Immunopharmacology</i> , Vol. 1, 2001, pgs. 1229-1234.
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Form 1449

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<b>FORM PTO-1449</b> U.S. Department of Commerce Patent and Trademark Office	<b>Docket No.</b> STEM1110-5	<b>Serial No.:</b> 10/050,190
<b>Applicants:</b> Twardzik et al.		
<b>SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>	<b>Filing Date:</b> January 15, 2002	<b>Group Art Unit:</b> 1647

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	DO	Zhang, Maobin et al., "Transforming Growth Factor $\alpha$ and a PC 12-Derived Growth Factor Induce Neurites in PC12 Cells and Enhance the Survival of Embryonic Brain Neurons," <i>Cell Regulation</i> , Vol. 1, June 1990, pgs. 511-521.
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